THYMIDINE KINASE MUTANTS AND FUSION PROTEINS HAVING THYMIDINE KINASE AND GUANYLATE KINASE ACTIVITIES

ABSTRACT OF THE DISCLOSURE

The present invention provides isolated nucleic acid molecules encoding a *Herpesviridae* thymidine kinase enzyme comprising one or more mutations, at least one of the mutations encoding an amino acid substitution located toward the N-terminus from a DRH nucleoside binding site which increases a biological activity of the thymidine kinase, as compared to unmutated thymidine kinase. Such mutations include amino acid substitutions within a Q substrate binding domain which increases a biological activity of the thymidine kinase, as compared to unmutated thymidine kinase. Within a further aspect, fusion proteins are provided which have both guanylate kinase and thymidine kinase biological properties. Also provided are vectors suitable for expressing such DNA molecules, as well as methods for utilizing such vectors.